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Declaration under Rule 4.17:
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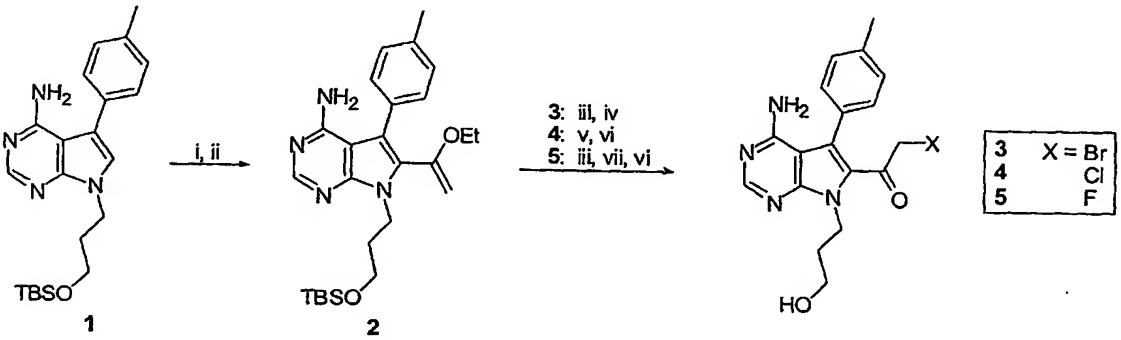
[Continued on next page]

(54) Title: SELECTIVE SERINE/THREONINE KINASE INHIBITORS



[a]Reagents and conditions: (i) NBS, DMF, rt (ii) $Pd(PPh_3)_4$, α-(ethoxyvinyl)tin, toluene, reflux. (iii) NBS, $NaHCO_3$, H_2O, DMF, -20 °C. (iv) 1:3 1N HBr:THF, 0 °C to rt. (v) NCS, $NaHCO_3$, H_2O, MeCN, rt. (vi) 1:3 1N HCl:THF, 0 °C to rt. (vii) KF, [bmim][BF_4], H_2O, MeCN, 60 °C.

(57) Abstract: Inhibition of protein kinases having one or more cysteine residues within the ATP binding site is effected by contacting the kinase, per se or in a cell or subject, with an inhibitory-effective amount of a compound having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of reacting with a cysteine residue within the ATP binding site of a kinase. Preferred compounds include certain pyrrolopyrimidines and oxindoles having such an electrophilic substituent and optionally an aromatic or heteroaromatic substituent that is capable of interacting with a threonine or smaller residue located in the gatekeeper position of the kinase. Kinases lacking such cysteine residues may be engineered or modified so that they are capable of being inhibited by such compounds by replacing a valine or other amino acid residue within the ATP binding site by a cysteine residue.

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